#### **DUTREIX** et al.

### U.S. National Phase of PCT/EP2004/012857

## **AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-15. (Cancelled)

16. (New) A nucleic acid molecule, wherein said molecule comprises a double stranded portion of at least 16 bp, has at least one free end, and wherein said molecule is substrate for binding by at least a Ku protein involved in the NHEJ pathway of double strand breaks repair.

17. (New) The molecule of claim 16, wherein said molecule comprises between 16 and 200 bp, more preferably between 24 and 100 bp.

18. (New) The molecule of claim 16, wherein said molecule is a linear or a hairpin nucleic acid molecule.

19. (New) The molecule of claim 18, wherein said molecule is a hairpin nucleic acid molecule and wherein the loop comprises nucleic acid or chemical groups.

20. (New) The molecule of claim 16, wherein at least one free end is blunt or 5'- or 3'-protruding.

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- 21. (New) The molecule of claim 16, wherein said molecule inhibits in vitro radiationenhanced illegitimate exogenous DNA integration.
- 22. (New) The molecule of claim 16, wherein said molecule is capable of being up-taken by cell into the cell nucleus.
- 23. (New) The molecule of claim 16, wherein said molecule comprises a phosphodiester backbone or a chemically modified phosphodiester backbone, or another backbone with one or several chemical groups.
- 24. (New) The molecule of claim 16, wherein said molecule comprises a 2'deoxynucleotide backbone, and optionally comprises one or several 2'-ribonucleotides
  or other modified nucleotides or nucleobases other than adenine, cytosine, guanine and
  thymine.
- 25. (New) The molecule of claim 23, wherein said backbone comprises methylphosphonates, phosphoramidates, morpholino nucleic acid, 2'-0,4'-C methylene/ethylene bridged locked nucleic acid, peptide nucleic acid (PNA), short chain alkyl, or cycloalkyl intersugar linkages or short chain heteroatomic or heterocyclic intrasugar linkages of variable length.

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- 26. (New) The molecule of claim 16, comprising one or several chemical groups at the end of each strand or, at least, at the 3' end strand.
- 27. (New) The molecule of claim 26, comprising one or several phosphorothicates at the end of each strand or, at least, at the 3'end strand.
- 28. (New) The molecule of claim 16, further comprising at least one embedded element, which hampers DNA replication, DNA repair, or damage signalling process, said at least one element being incorporated in the centre or at the end of the double-stranded molecule.

### 29. (New) The molecule of claim 28, comprising

- a) a polyethyleneglycol chain, preferably a hexaethyleneglycol chain, or any hydrocarbon chain, optionally interrupted and/or substituted by one or more heteroatoms e.g., oxygen, sulfur, nitrogen, or heteroatomic or heterocyclic groups, comprising one or several heteroatoms;
- b) a unit which is a blocking element as it is not amenable by DNA polymerases or exonucleases, such as any 3'-modified nucleotides,
- c) a native oligonucleotide, such as Tn, when used in the loop of an hairpin fragment, preferably a tetradeoxythymidylate (T4).

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- 30. (New) The molecule of claim 16, wherein said molecule is made by chemical synthesis, semi-biosynthesis or biosynthesis.
- 31. (New) A molecule selected from DRIL32, DRIL32po-PEG, DRIL32-PEG, DRIL16-PEG, DRIL32-T4, DRIL32-2xPEG, DRIL32s33-PEG, DRIL32-NH2, DRIL32-FITC, DRIL32-Cy3, DRIL32-Bt, DRIL64 and DRIL64-PEG.
- 32. (New) A method of enhancing tumor sensitivity to DNA damaging anticancer therapy, the method comprising administering to a subject a molecule of claim 16.
- 33. (New) A method of treating cancer, the method comprising administering to a subject a molecule of claim 16 in combination with a DNA damaging anticancer therapy.
- 34. (New) The method of claim 33, wherein the DNA damaging anticancer therapy is selected from radiotherapy and chemotherapy.
- 35. (New) The method of claim 34, wherein the molecule is administered prior to radiotherapy.
- 36. (New) The method of claim 34, wherein the molecule is administered prior to or along with chemotherapy.

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- 37. (New) The method of claim 32, wherein the cancer is selected from glioblastoma, breast cancer and cervical cancer.
- 38. (New) The method of claim 32, wherein the molecule is administered by intravenous, intra-tumoral or sub-cutaneous injection, or by oral route.
- 39. (New) A composition for use in association with a DNA breaking treatment, particularly radiotherapy or chemotherapy, said composition comprising at least one molecule of claim 16 in combination with a pharmaceutically acceptable carrier, in an efficient amount to be introduced in the nucleus of tumor cells.